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HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

FINAL SUBMISSION

For

POLYBUTYLENE SUCCINIC ANHYDRIDES

Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental, and Regulatory Task Group

December 2005

LIST OF MEMBER COMPANIES IN THE HEALTH, ENVIRONMENTAL, AND REGULATORY TASK GROUP

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel includes the following member companies:

Afton Chemical Corporation (formerly Ethyl Corporation)

Chevron Oronite, LLC

ExxonMobil Chemical Company

Infineum

The Lubrizol Corporation

SNPE

EXECUTIVE SUMMARY

The American Chemistry Council Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its member companies, hereby submit for review and public comment their final submission for the *"Polybutylene Succinic Anhydride"* category of chemicals under the United States Environmental Protection Agency High Production Volume (HPV) Chemical Challenge Program. This submission should be read in its entirety in order to obtain an understanding of the chemical category.

Polybutylene Succinic Anhydride Category. The following two closely related high molecular weight polymers (>1,000 grams/mole) constitute a chemical category:

- 2,5-Furandione, dihydro-, monopolyisobutylene derivs., (CAS #67762-77-0), referred to as "Polyisobutylene succinic anhydride".
- 2,5-Furandione, dihydro-, monopolybutenyl derivs., (CAS #67762-79-2), referred to as "Polybutenyl succinic anhydride".

Fate and Transport Characteristics. A member of this category, polyisobutylene succinic anhydride, has been shown to have limited biodegradability. Existing information for the anhydrides suggests that the polybutylene succinic anhydrides will undergo hydrolysis and will be the form that should be considered when evaluating environmental fate. Direct photodegradation is not expected to cause significant physical degradation of members in this category. Modeled data showed that there is a low likelihood of (OH-) radical attack. These substances are not expected to significantly partition to air if released into the environment because of their relatively low vapor pressure. Level III fugacity modeling illustrated the polybutylene succinic anhydrides are likely to partition primarily in the soil and sediment.

Aquatic Toxicology. Data are available to adequately characterize fish, invertebrate and alga toxicity, indicating a low concern for aquatic effects.

Mammalian Toxicology - Acute. Data on acute mammalian toxicity are available for both members of the category and were reviewed and the findings indicate a low concern for acute toxicity.

Mammalian Toxicology – Subchronic and Reproductive/Developmental Toxicity. Significant evidence in the literature indicates that members of the polyisobutylene succinic anhydride category are too large and hydrophobic to be absorbed in the intestinal lumen. As a result, the polybutylene succinic anhydrides likely possess minimal toxicity in repeated-dose and reproductive/developmental toxicity studies. Additionally, members of the polyisobutylene succinic anhydride category will be present in water as succinic acid derivatives. The importance and consumption of succinic acids in the Krebs cycle and fatty acid metabolism further illustrates that the members of the polyisobutylene succinic anhydride category are polymers of low toxicological concern.

Mammalian Toxicology - Mutagenicity. Data from bacterial reverse mutation assays are available for both members of the polyisobutylene succinic anhydride category and showed the both materials are not mutagenic. As mentioned above, the members of the polyisobutylene succinic anhydride category are too large to penetrate a membrane, thus combined with the negative Ames results for each material; the polybutylene succinic anhydrides are unlikely to cause chromosomal aberrations.

Conclusion. Based upon the data reviewed for this final submission and publicly available literature, the members of the polyisobutylene succinic anhydride category are likely to partition to the soil and sediment, not readily biodegradable but possess little to no toxicity to aquatic or mammalian organisms.

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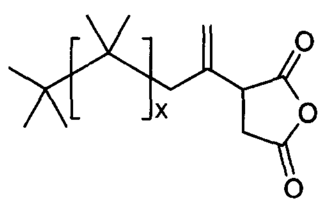
1.0 INTRODUCTION

In March 1999, the American Chemistry Council (formerly the Chemical Manufacturers Association) Petroleum Additives Panel Health, Environmental and Regulatory Task Group (HERTG), and its participating member companies committed to address data needs for certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This final submission follows up on that commitment.

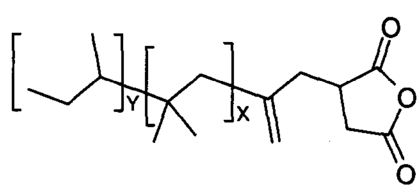
Specifically, this final submission sets forth how the HERTG addressed physiochemical, environmental, aquatic and health effects testing information for the following two high molecular weight polymers:

- 2,5-Furandione, dihydro-, monopolyisobutylene derivs., (CAS #67762-77-0), referred to as "Polyisobutylene succinic anhydride".
- 2,5-Furandione, dihydro-, monopolybutenyl derivs., (CAS #67762-79-2), referred to as "Polybutenyl succinic anhydride".

FIGURE 1. CHEMICAL STUCTURES



CAS # 67762-77-0
2,5-Furandione, dihyro-,monopolyisobutylene derivs.
X =18 - 41
PIB MW = 1000 - 2500



CAS # 67762-79-2
2,5 - Furandione, dihydro-, monopolybutenyl derivs.
X = 18 - 41
PB MW = 1000 - 2500

In preparing this Final Submission dossier, the following steps were undertaken:

Step 1: A review of the literature and confidential company data was conducted on the physiochemical properties, mammalian toxicity endpoints, and environmental fate and effects for the polybutylene succinic anhydrides. Searches included the following sources: MEDLINE, BIOSIS, CANCERLIT, CAPLUS, CHEMLIST, EMBASE, HSDB, RTECS, EMIC, and TOXLINE databases; the TSCATS database for relevant unpublished studies on these chemicals; and standard handbooks and databases (e.g., Sax, CRC Handbook on Chemicals, IUCLID, Merck Index, and other references) for physiochemical properties.

Step 2: The compiled data was evaluated for adequacy in accordance with the EPA guidance documentation.

2.0 GENERAL SUBSTANCE INFORMATION

2.1 Manufacture Of Polybutylene Succinic Anhydrides

Polybutylene succinic anhydrides are amphiphilic molecules, wherein the hydrophobic polybutylene polymer is attached chemically to a hydrophilic succinic anhydride group. These substances are produced from the reaction of polybutylene polymers and maleic anhydride to give polybutylene succinic anhydride. At the end of the reaction, the unreacted maleic anhydride is stripped out of the mixture containing polybutylene succinic anhydride, but the unreacted polybutylene polymer remains in the mixture.

2.2 Use Of Polybutylene Succinic Anhydrides

Polybutylene succinic anhydrides are commonly used as either components or as intermediates in the manufacture of oil soluble dispersants for lubricants, anti-rust additives and emulsifiers. The finished lubricating oils include all types of internal combustion engine oils (e.g., automotive and diesel engine crankcase oils, air and water-cooled two-cycle engine oils, natural gas engine oils, marine trunk piston engine oils, medium-speed railroad diesel engine oils), automatic transmission fluids, and gear oils. They are used as ashless dispersant intermediates to inhibit colloidal particle-to-particle aggregation by an adsorbed film mechanism and they solubilize oil-insoluble liquids. Polybutylene succinic anhydride dispersant intermediates are generally sold to finished oil blenders in additive packages where the concentration ranges typically from 5 to 50 wt.%. These additive packages are then blended into finished oils where the typical concentration of polybutylene succinic anhydride dispersant ranges from 0.5 to 10 wt.% in the finished oil depending on the application.

3.0 PHYSICOCHEMICAL PROPERTIES OF POLYBUTYLENE SUCCINIC ANHYDRDIDES

Selected physicochemical properties of members from the polybutylene succinic anhydride category are presented in Table 1.

TABLE 1. PHYSICOCHEMICAL PROPERTIES

CAS Number	Molecular Weight	Melting Point[1] (°C)	Boiling Point[2] (°C)	Vapor Pressure[3] (Pa)	Water Solubility[11] (mg/L)	Log Kow
67762-77-0	519 to 2483*	188.46	476.62	2.07e-009	NA[5]	NA[6]
		349.84	1695.4	0.0	0.0	NA[6]
67762-79-2	500 to 2500*	ND	ND	3e-4	NA[6]	NA[10]
		ND	ND	ND	NA[6]	NA[10]

[1] Modeling data; melting point is estimated (MPBWIN v1.40), viscosity of liquid prevents measurement.
[2] Modeling data; boiling point is estimated (MPBWIN v1.40) and cannot be measured because these substances decompose before they boil.
[3] Modeling data; vapor pressure is estimated (MPBPWIN v1.40).
[5] Not applicable; anhydrides form diacids in aqueous solutions, the water solubility of the diacid of CAS #67762-77-0[6] is calculated to be 1.671e-01 mg/L to 0.0.
[6] Not applicable; anhydrides form diacids in aqueous solutions (diacid Log Kow calculated: 14.65-77.95).
[10] Not applicable; anhydrides form diacids in aqueous solutions.
[11] Modeling data; water solubility is estimated (KOWWIN v1.65).
ND = Not determined.
* In the applications used by members of the ACC HERTG, the molecular weight is >1000.

4.0 ENVIRONMENTAL FATE DATA FOR THE POLYBUTYLENE SUCCINIC ANHYDRIDES

4.1 Biodegradation

One member of the polybutylene succinic anhydride category has been tested. The Modified Sturm Test (OECD Guideline 301B, *CO_2 Evolution Test*) was used to evaluate the biodegradability of polyisobutylene succinic anhydride (CAS # 67762-77-0). After the 28-day test, the extent of biodegradation was 2.3-5.0% based on carbon dioxide evolution. These results were bridged to the other group member.

4.2 Fugacity Modeling

All of the members of this category have low vapor pressure and are sparingly water soluble suggesting that they will not tend to partition into the air or water to any great extent. Level III Fugacity modeling indicated that the polybutylene succinic anhydride molecules will readily partition to the soil and sediment (Table 2).

4.3 Hydrolysis

Polybutylene succinic anhydrides contain a functional group that has the potential to hydrolyze. Polybutylene butanedioic acid is the hydrolysis product of this anhydride.

This reaction is believed to occur at a rapid rate. Industrial experience indicates that addition of the polybutylene succinic anhydrides to water results in the polybutylene succinic acid derivatives. This rapid hydrolysis of the anhydride moiety is supported by data indicated that succinic anhydrides in general, readily hydrolyze to the corresponding succinic acid (Furia, T.E., 1972).

4.4 Photodegradation

Members of the polybutylene succinic anhydride category do not contain bonds that have a high potential to absorb UV light above 290 nm. Further, these substances have low vapor pressure, which indicates that they have a low potential to partition into the air to a significant extent where they would be subject to indirect photodegradation. Modeled photodegradation data (Table 2; EPIWIN), further illustrates the group 27 materials have a very low likelihood of photodegradation.

TABLE 2. ENVIRONMENTAL FATE DATA FOR THE POLYBUTYLENE SUCCINIC ANHYDRIDES CATEGORY

CAS Number	PHOTODEGRADATION[1]	FUGACITY[1] (partitioning)
67762-77-0 MW = 1009 g	OH- Rate Constant: 77.01 x 10-12 cm^3/moles-sec Half life (days) = 0.139	Air : 0.011 % Water : 0.727 % Soil : 41.1 % Sediment : 58.2 %
67762-79-2 MW = 996 g	OH- Rate Constant: 77.01 x 10-12 cm^3/moles-sec Half life (days) = 0.139	Air : 0.011 % Water : 0.727 % Soil : 41.1 % Sediment : 58.2 %

[1] Photodegradation and fugacity endpoints were modeled using the EPIWIN version 3.12 software.

5.0 AQUATIC TOXICITY DATA FOR THE POLYBUTYLENE SUCCINIC ANHYDRIDES

Adequate acute aquatic ecotoxicity studies have been conducted for the polybutylene succinic anhydride category. These studies involved three trophic levels of aquatic organisms and evaluated the acute aquatic ecotoxicity of one of the two members of the category. The data demonstrate a low order of acute aquatic ecotoxicity, and can be used for bridging to the remaining category member (polybutenyl succinic anhydride, CAS #67762-79-2).

5.1 Fish Acute Toxicity

Polyisobutylene succinic anhydride (CAS #67762-77-0) was evaluated for acute toxicity to fish. The maximum test material loading rate was 1,000 mg/L. Mortality of 10 to 25% was observed at loading rates greater than 600 mg/L after 96 hours, and a loading rate-response relationship was apparent. The LL_{50} for this substance was greater than 1,000 mg/L, indicating a low order of toxicity to fish.

5.2 Invertebrate Acute Toxicity

Polyisobutylene succinic anhydride (CAS #67762-77-0) was evaluated for acute toxicity to daphnids (*Daphnia magna*). The single (maximum) test material loading rate was 1,000 mg/L. No mortality of *D. magna* occurred within the 48-hour exposure. The EL_{50} for this substance was greater than 1,000 mg/L, and the EL_0 determined in the test was 1,000 mg/L, indicating a low order of toxicity to aquatic invertebrates.

5.3 Alga Toxicity

Polyisobutylene succinic anhydride (CAS #67762-77-0) was evaluated for effects on the growth of the unicellular green alga, *Pseudokirchneriella subcapitata*, in a 96-hour exposure. The single (maximum) test substance loading rate was 1,000 mg/L. No inhibition of algal cell density was observed. The EL_{50} for this substance was greater than 1,000 mg/L.

Table 3. Aquatic Toxicity Data for Polybutylene Succinic Anhydride Category

CAS Number	**ACUTE TOXICITY TO FISH 96-hr LC_{50} (mg/L)**	**ACUTE TOXICITY TO INVERTEBRATES 96-hr LC_{50} (mg/L)**	**TOXICITY TO ALGAE 96-hr EC_{50} (mg/L)**
67762-77-0	LL_{50} >1000 mg/L (WAF, RT)	EC_{50} >1000 mg/L (WAF, DM)	EC_{50} >1000 mg/L (WAF, PK)
67762-79-2	No testing Bridging	No testing Bridging	No testing Bridging

WAF = Water Accommodated Fraction
RT = Rainbow Trout
DM = *Daphnia magna*
PK = *Pseudokirchneriella subcapitata*

6.0 MAMMALIAN TOXICITY DATA OF POLYBUTYLENE SUCCINIC ANHYDRIDES

6.1 Acute Mammalian Toxicity

Acute toxicity data for the polybutylene succinic anhydride category is summarized in Table 4. Both members of the category have been tested by the oral and dermal route of administration and demonstrated a low order of acute toxicity.

6.1.1 Acute Oral Toxicity

The two substances in the polybutylene succinic anhydride category have been adequately tested for acute oral toxicity. The acute oral LD_{50} for these studies in rats is greater than 2000 mg/kg indicative of a low order of acute toxicity (Table 4).

6.1.2 Acute Dermal Toxicity

The two substances in the polybutylene succinic anhydride category have been adequately tested for acute dermal toxicity. The acute dermal LD_{50} for this study in rabbits was greater than 2000 mg/kg indicative of a low order of acute toxicity (Table 4).

TABLE 4. ACUTE MAMMALIAN TOXICITY DATA FOR MEMBERS OF THE POLYBUTYLENE SUCCINIC ANHYDRIDE CATEGORY

CAS Number	ACUTE ORAL TOXICITY[1] Available Data	ACUTE DERMAL TOXICITY[1] Available Data
67762-77-0	LD_{50} > 2.0 g/kg (rat)	LD_{50} > 2.0 g/kg (rabbit)
67762-79-2	LD_{50} > 2.0 g/kg (rat)	LD_{50} > 2.0 g/kg (rabbit)

[1]Toxicity endpoints are expressed as median lethal dose (LD_{50}) for acute oral and dermal toxicity.

6.2 Repeated-dose and Reproductive/Developmental Toxicity

Lipinski et al., (1997) identified physical characteristics that influence the solubility and absorption across the intestinal lumen by evaluating more than 2200 drug development tests. The data illustrated that materials possessing a molecular weight of greater than 500 grams/mole and a log P of greater than 5 had only minimal absorption across the intestinal lumen. These findings were rigorously tested in later papers (Wenlock et al., 2003; Veith et al, 2004;

Proudfoot, 2005). Both of the members of the polyisobutylene succinic anhydride category have a molecular weight greater than 1000 grams/mole and the log P (and log Kow) values were calculated to be greater than 10 (log P values were determined using the ChemOffice software). Therefore, based on the molecular weights and Log P values, the polybutylene succinic anhydrides will not be readily absorbed in the intestinal lumen and as a result, would not possess significant repeated-dose or reproductive/developmental toxicity. The low anticipated repeated-dose toxicity of the polybutylene succinic acids is supported by the high acute oral LD_{50}s for both members of the polyisobutylene succinic anhydride category.

As mentioned above, the polybutylene succinic anhydrides are present in aqueous solutions as succinic acid derivatives. In this regard, the low anticipated toxicity to mammals of the members of the polyisobutylene succinic anhydride category is further supported by the low toxicity of succinic acid. In the HPV dicarboxylic acid category made by DuPont, rats were exposed to extremely high doses of succinic acid (high doses of approximately 3865, 7730, and 15,460 mg/kg/day) for 13 weeks. Weight loss occurred at the mid and high doses which was probably a result of palatability issues or gastric irritation from the large dicarboxylic acid load. There was some mortality at the high dose which may have been a result of the weight loss, gastric hemorrhage or a combination of the two problems. The robust summary associated with DuPont's dicarboxylic test plan lacks sufficient detail to assign cause to the mortalities. Despite deaths at the highest dose, the only adverse effect at the other doses was severe weight loss.

6.3 Mutagenicity

6.3.1 Bacterial Gene Mutation Assay

Both substances in this category have been adequately tested in a bacterial reverse mutation test (OECD Guidelines 471 and/or 472). Both tested substances were negative for mutagenic activity, with and without metabolic activation.

6.3.2 *In Vitro* Chromosomal Aberrations

Based on the Ames assay results described above and the likely inability of polybutylene succinic anhydrides to cross cell membranes (due to their high molecular weights and high log P values), the members of the polyisobutylene succinic anhydride category are unlikely to cause chromosomal aberrations.

7.0 TOXICITY SUMMARY OF POLYBUTYLENE SUCCINIC ACIDS

Based on data and evidence from the literature, both members of the polyisobutylene succinic anhydride category represent large molecular weight polymers of low toxicological concern. These materials have molecular weights above 1000, do not contain charged monomers, and there is less than 25% of the material present below 1000 grams. The low toxicity of these materials further supports the EPA's rationale for exempting polymers of this size/nature from testing (EPA, 1997).

REFERENCES

Ain, R., and P.B. Seshagiri. 1997. Succinate and Malate Improve Development of Hamster Eight-Cell Embryos *In Vitro*: Confirmation of Viability of Embryo Transfer. Mol. Reprod. Dev. 47: 440-447.

Comber, M., S. Robertson, and Sijm D. DRAFT Discussion paper for the TC NES subgroup on PBTs. Appendix for ECETOC, Alternative Testing Methods in Environmental Sciences.

Du Pont de Nemours & Co, Inc & Solutia, Inc. Dicarboxylic Acid Test Plan. Submitted to the Environmental Protection Agency. July 11, 2001. Available at http://www.epa.gov/chemrtk/dicarbx/c13108cv.htm

Environmental Protection Agency (1997) Polymer Exemption Guidance Manual. Office of Pollution Prevention and Toxics.

Furia, T.E., Ed. 1972. CRC Handbook of Food Additives. 2nd Edition. Cleveland: The Chemical Rubber Co., p. 232.

Lipinski *et al.* 1997. Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings. Adv. Drug Delivery Rev. 23: 3-25.

Opperhuizen, A. *et al.* 1987. Uptake and Elimination by Fish of Polydimethylsiloxanes (Silicones) After Dietary and Aqueous Exposure. Toxicol. Env. Chem. 13, 265-285.

Proudfoot, J.R. 2005. The Evolution of Synthetic Oral Drug Properties. Bioorg. Med. Chem. Lett. 15: 1087-1090.

U.S. Environmental Protection Agency. 2004. EPI Suite v3.12. Available at http://www.epa.gov/opptintr/exposure/docs/updates_episuite_v3.12.revised.htm

Vieth, M. *et al.* 2004. Characteristic Physical Properties and Structural Fragments of Marketed Oral drugs. J. Med. Chem. 47: 224-232.

Verrett, M.J., *et al.* 1980. Toxicity and Teratogenicity of Food Additive Chemicals in Developing Chicken Embryo. Toxicol. App. Pharmacol. 56: 265-273.

Wenlock, M.C., *et al.* 2003. A Comparison of Physiochemical Property Profiles of Development and Marketed Oral Drugs. J. Med. Chem. 46: 1250-1256

Yanagihara T, *et al.* 2005. Electrolyzed Hydrogen-Saturated Water for Drinking Use Elicits and Antioxidative Effect: A Feeding Test with Rats. Biosci. Biotechnol. Biochem. 69: 1985-1987.